



# **Armed Forces College of Medicine AFCM**



# **Neuropathic Pain, Pain ,control system Sensory cortex and Sensory lesions**

**Ass. Prof. Doaa Abou-bakr**

# INTENDED LEARNING OBJECTIVES (ILO)



**By the end of this lecture the student will be able to:**

1. Describe neuropathic pain
2. Explain the endogenous control of pain sensations
3. Describe stress analgesia
4. List the somatosensory areas of the cortex
5. Describe the organization, body presentation and functions of each one
6. Explain the consequences of their lesions
7. Explain the pathophysiology of different sensory lesions as syringomyelia, herpes zoster, peripheral neuropathy and sensory ataxia

# Lecture Plan



1. Part 1 (5 min) **Introduction**
2. Part 2 (35 min) **Main lecture:**
  - 1. Neuropathic pain**
  - 2. Pain analgesia system**
  - 3. Somatosensory cortex**
  - 4. Sensory lesions**
3. Part 3 (5 min) **Summary**
- 4. Lecture Quiz (5 min)**

# Neuropathic pain



- Is a **chronic** pain.
- Occurs when **nerve** fibers are injured.
- It is **excruciating**, and it is a difficult condition to treat.
- The resulting pain **lasts much longer than the injury itself**.
- The pain is often accompanied by **hyperalgesia** and **allodynia**.

# Neuropathic pain



- **Hyperalgesia** is an exaggerated response to a noxious stimulus.
- **Allodynia** is a sensation of pain in response to a normally innocuous stimulus. An example is the painful sensation from a warm shower when the skin is damaged by sunburn.

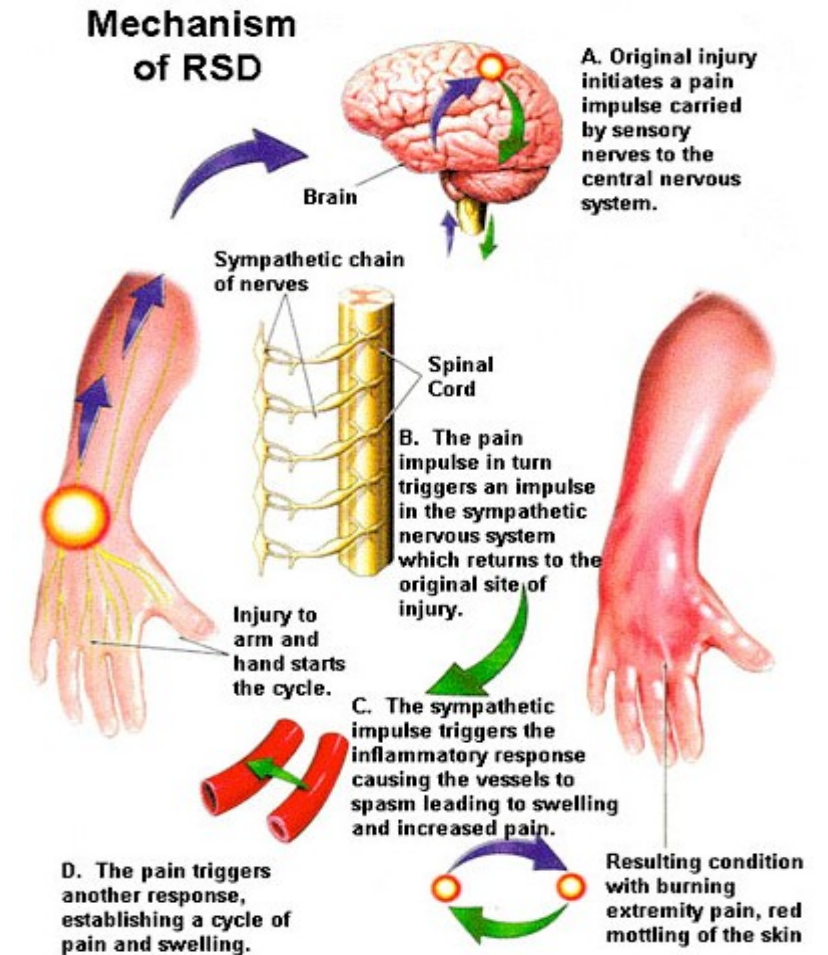
**Hyperalgesia and allodynia  
signify increased sensitivity of  
nociceptive afferent fibers.**

# Neuropathic pain



## Examples:

- Post herpetic (post-shingles) neuralgia.
- Phantom limb pain.
- Entrapment neuropathy (e.g. carpal tunnel syndrome).
- Reflex sympathetic dystrophy (RSD)/ causalgia (a spontaneous burning pain occurs long after trivial nerve trauma).
- Peripheral neuropathy.



**Causalgia / RSD**

# Neuropathic pain (Quiz)



**Complete:**

**e:**

➤ **Hyperalgesia** is ..... response to ..... stimulus.

exaggerated

noxious

pain

Innocuous

➤ **Allodynia** is ..... in response to ..... stimulus.



# Pain modulation (modification)



## •Exaggeration (Facilitation);

- Pathological
- e.g. cutaneous hyperalgesia and thalamic syndrome.

## •Inhibition (Suppression);

- Physiological
- Pain analgesia system.

# Pain analgesia system



- **Spinal control** = peripheral control  
(Gate theory)

- **Supraspinal control** = central control  
(Descending pathway)

# Spinal control= peripheral control (Gate theory)



- **Theory:**

there are many relay stations (synapses) in the sensory pathway of pain that act as a gate to be open or close.

- **Gates: 3**

**1.Spinal gate** (substantia gelatinosa of relandi = SGR) = site of relay of 1<sup>st</sup> order neuron.

**2.Thalamic gate** = site of relay of 2<sup>nd</sup> order neuron.

**3.Reticular gate** (reticular formation) = site of relay of 2<sup>nd</sup> order neuron.

# Spinal control= peripheral control (Gate theory)



**Spinal gate:** At SGR, pain transmission can be blocked by:

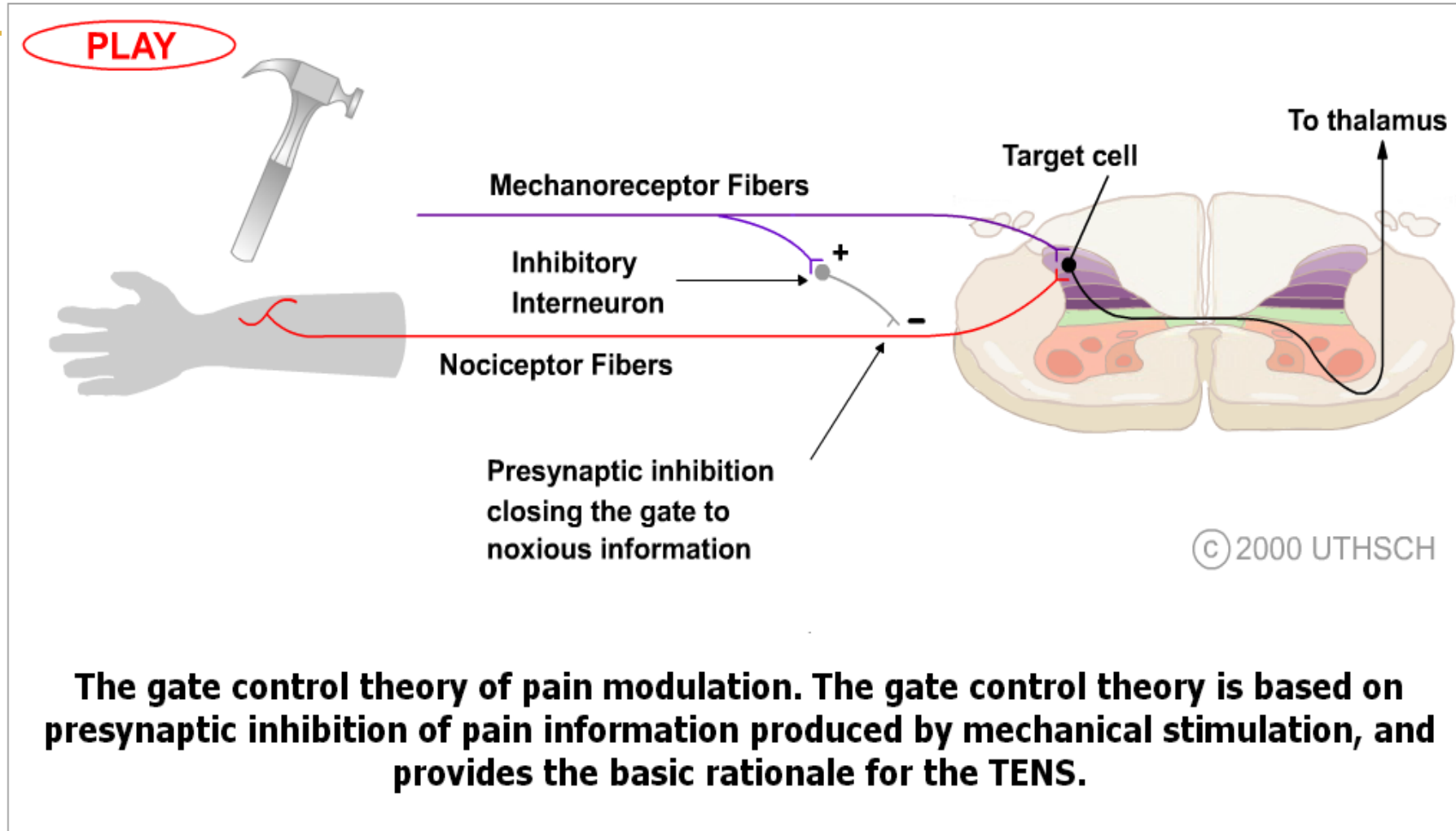
- 1. Collaterals from thick myelinated A $\beta$  fibers of dorsal column tract:** stimulation of these sensory fibers by tactile stimuli (rubbing the skin, applying liniments near painful area).
- 2. Collaterals from A $\delta$  fibers of spinothalamic tract:** stimulation of these sensory fibers by counterirritant or acupuncture.
- 3. Descending fibers (corticofugal or centrifugal or centripetal):** stimulation of these fibers by psychogenic excitation of central analgesia system.

**N.B.:**

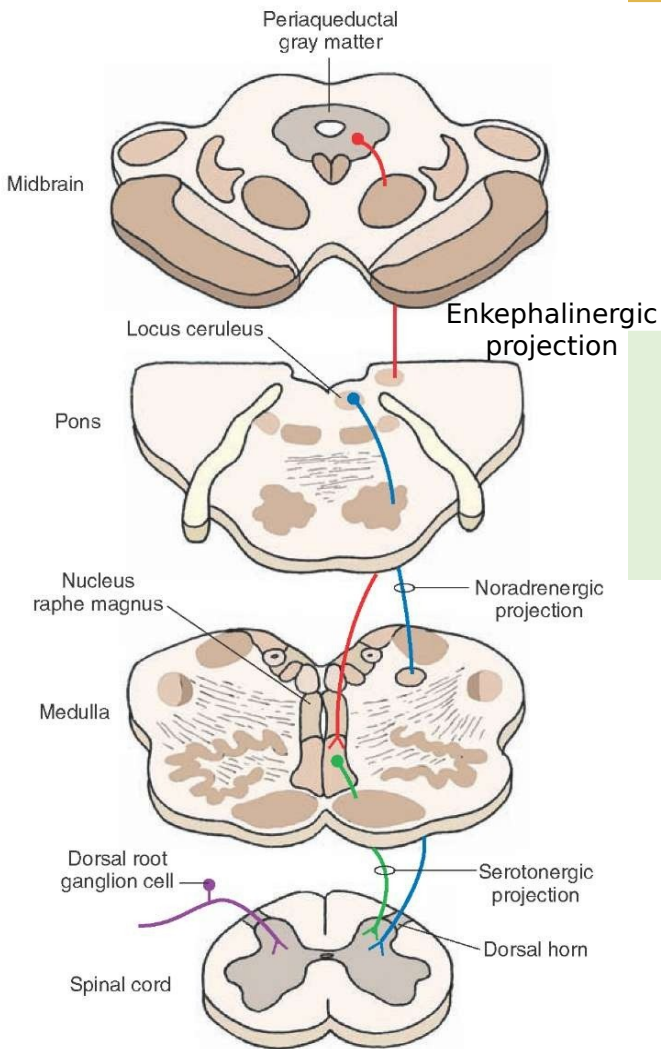
- All act by presynaptic inhibition (GABA or Enkephalin)**



# Spinal control= peripheral control (Gate theory)



# Supraspinal control= central control (Descending pathway)

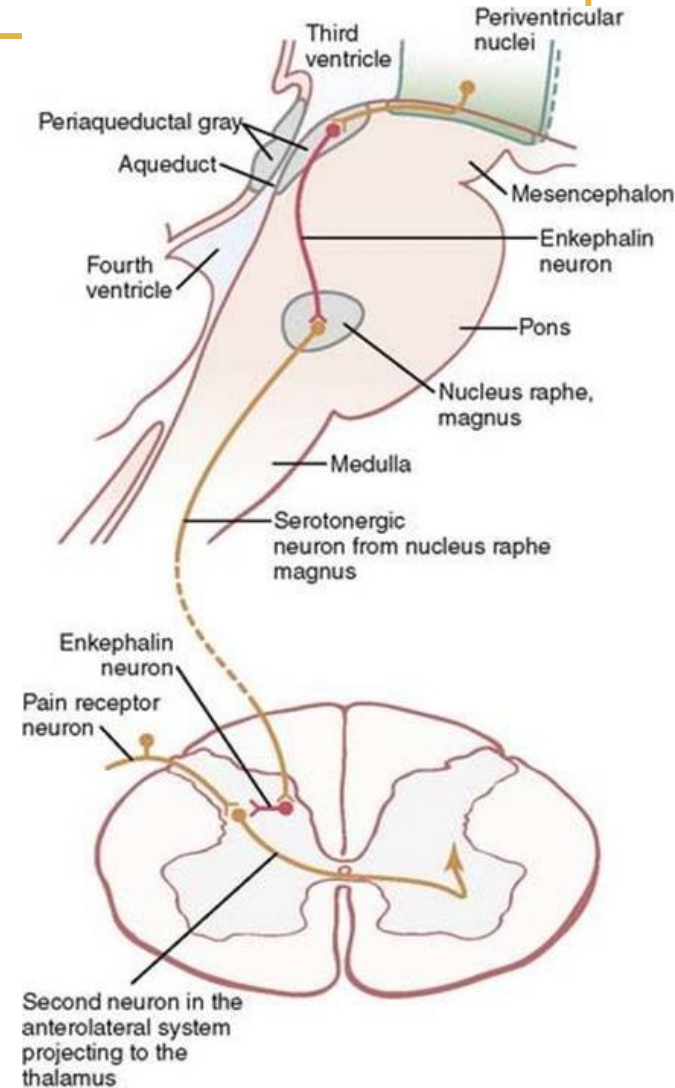


**Periaqueductal Gray Matter (PAG)**  
at midbrain  
**enkephalinergic fibers**

**Raphe Magnus Nucleus (RMN)**  
at medulla  
**Serotonergic fibers**

**Locus Ceruleus**  
at upper pons  
**Noradrenergic fibers**

**Pain Inhibitory Complex (PIC)**  
at the dorsal horn of spinal cord  
**enkephalinergic interneurons**



# Supraspinal control= central control (Descending pathway)



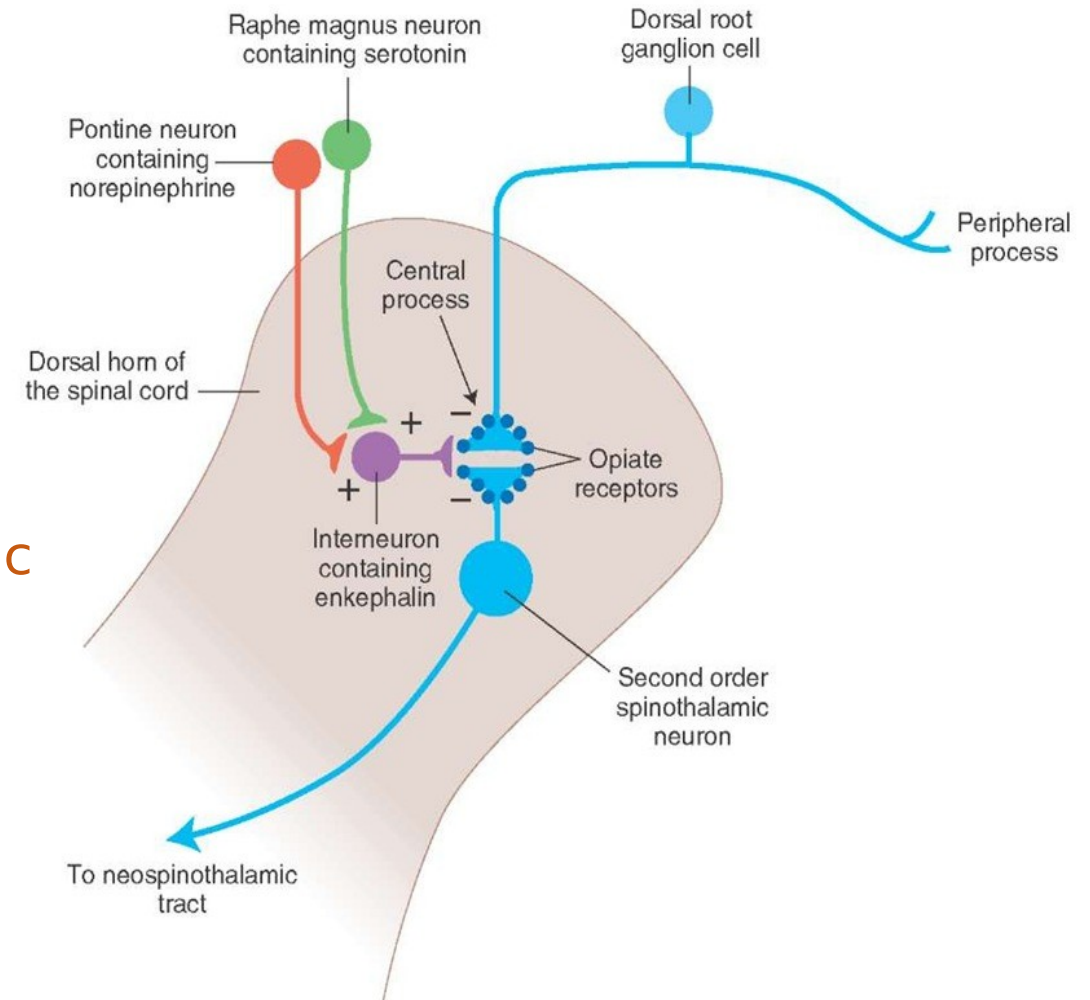
**PIC** form synapse with pain mediating neurons:

1. **Axo-axonal type** synapses on the 1<sup>st</sup> order (afferent) terminals of pain fibers.
2. **Axo-dendritic type** synapses on the 2<sup>nd</sup> order (dorsal horn) neurons.

Stimulation of the descending **serotonergic projections from the raphe magus**, **noradrenergic projections from locus ceruleus** excite **enkephalinergic interneurons** in the spinal cord. Enkephalins released from these interneurons inhibit:

3. The release of transmitter from the central processes of nociceptive dorsal root ganglion neurons (**presynaptic inhibition**).

4. The second order spinothalamic dorsal horn neurons (**postsynaptic inhibition**).







# Clinical applications



**Morphine injection** is used to relieve pain by acting on its receptors in the pain analgesia system.

**Electrical stimulation** of PAG and RMN in human subjects and experimental animals is known to suppress the activity of nociceptive mechanisms (i.e., analgesia is produced).

**Acupuncture** relieves pain by:

1. activation of spinal pathway of pain inhibition through activation of A $\delta$  fibers.
2. psychogenic excitation of cerebral analgesia system.

**The inhibitory effect of enkephalins are mediated by affecting K<sup>+</sup>, Ca<sup>2+</sup> flux. By binding to its receptors, dissociation of G $\alpha$  and G $\beta\gamma$  subunits. The G $\alpha$  directly interact with inward rectifying potassium channels causing hyperpolarization. The G $\alpha$  also inhibits adenylate cyclase activity, which decrease the formation of cAMP, thus reducing the cAMP-dependent calcium influx. The G $\beta\gamma$  further reduces calcium influx by directly binding to various classes of Ca<sup>2+</sup> channels.**



# STRESS- ANALGESIA



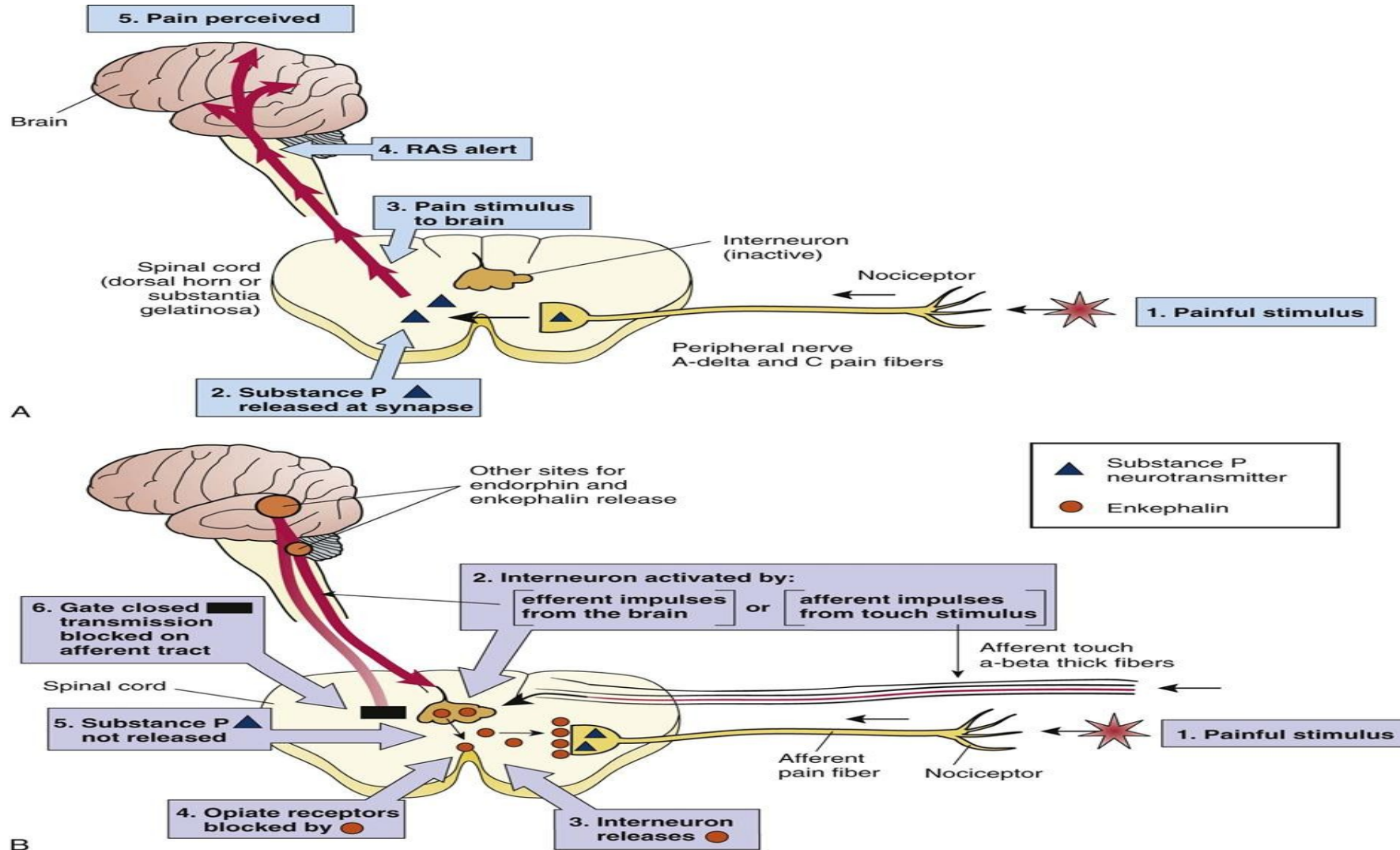
**Definition:** Reduced pain sensitivity when being attacked by a predator or other stressful events.

**Example:** It is well known that soldiers wounded in the battle often feel no pain until the battle is over. **Mechanism:**

- Impulses from cerebral cortex (limbic lobe) and hypothalamus (periventricular nucleus; PVN): fibers releasing endorphin to stimulate the PAG.
- $\beta$ -endorphin released in blood from anterior pituitary.



# Pain and Supraspinal pain control



# Pain analgesia system (Quiz)



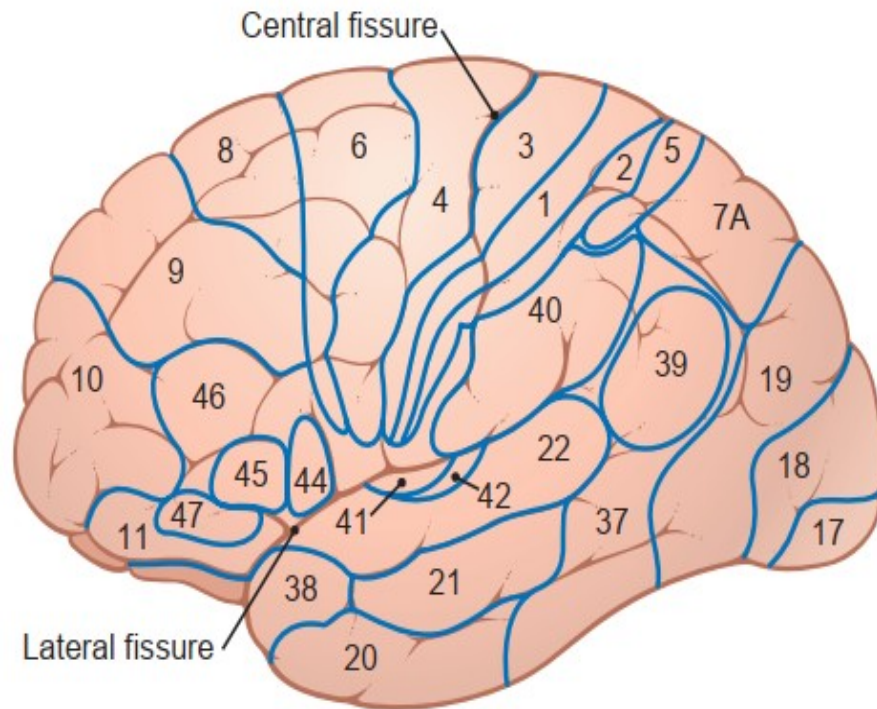
**Which of the following CNS regions is correctly paired with a neurotransmitter or a chemical involved in pain modulation?**

- A. Periaqueductal gray matter and serotonin
- B. Nucleus raphe magnus and norepinephrine
- C. Spinal dorsal horn and enkephalin
- D. Dorsal root ganglion and opioids
- E. Spinal dorsal horn and endorphin

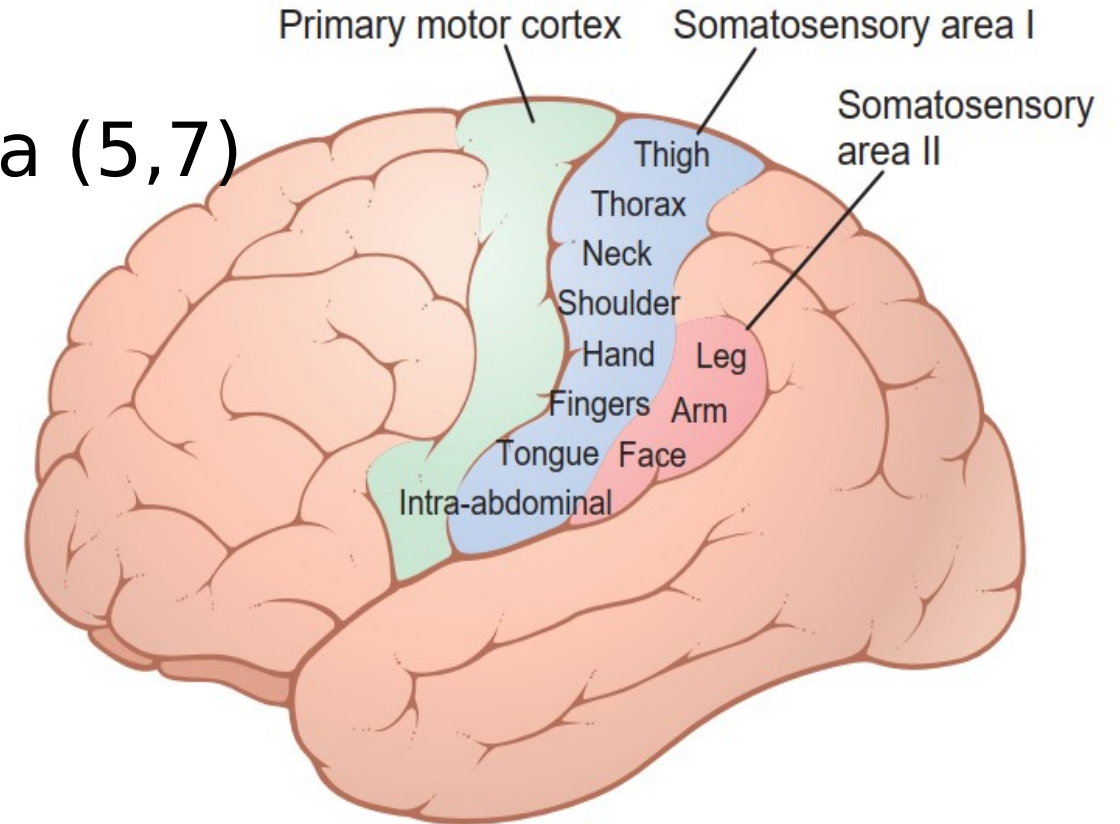
# SOMATOSENSORY CORTEX



- Somatosensory area I (1,2,3)
- Somatosensory area II (40)
- Somatosensory association area (5,7)



**Brodmann's areas**

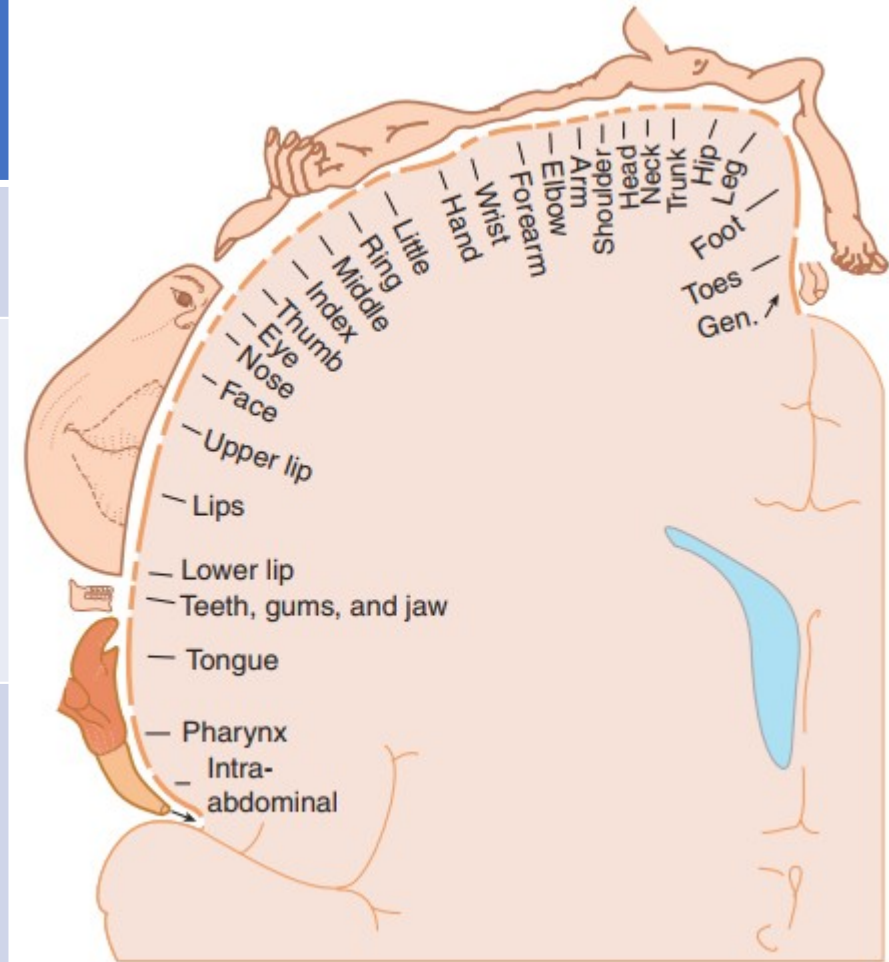


**Somatosensory Areas I and II**

# Somatosensory area I (SI)



<b>Location</b>	in the parietal cortex immediately behind the central fissure, located in the postcentral gyrus
<b>Brodmann's areas</b>	1, 2, and 3
<b>Body representation</b>	<ul style="list-style-type: none"> <li>-Crossed</li> <li>-Inverted</li> <li>-The sizes of the represented parts are directly proportional to the number of sensory receptors in each respective peripheral area of the body.</li> </ul>
<b>Effect of its lesion</b>	<p>Contralateral loss of fine (epicritic) sensations:</p> <ol style="list-style-type: none"> <li>1. Tactile localization and discrimination.</li> <li>2. Pressure (To judge the weights of objects).</li> <li>3. Vibration.</li> <li>4. Proprioception.</li> <li>5. Stereognosis (To judge shapes or forms of objects). This condition is called <b>astereognosis</b></li> </ol>



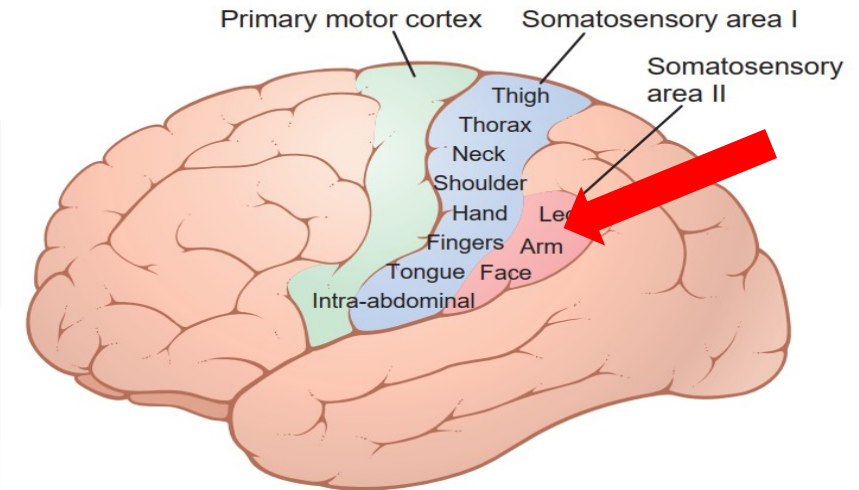
**Sensory Homunculus.** Representation of the different areas of the body in somatosensory area I of the cortex.



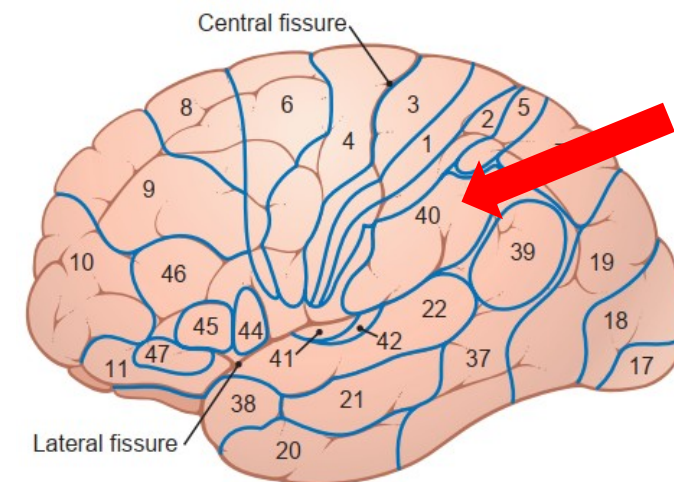
# Somatosensory area II (SII)



<b>Location</b>	<b>in the parietal cortex immediately behind the lower part of somatosensory area I.</b>
<b>Brodmann's areas</b>	40
<b>Body representation</b>	<ul style="list-style-type: none"> <li>-The face is represented anteriorly, the arms centrally, and the legs posteriorly.</li> <li>-Poor localization</li> </ul>
<b>Effect of its lesion</b>	Projections from somatosensory area I are required for function of somatosensory area II. However, removal of parts of somatosensory area II has no apparent effect on the response of neurons in somatosensory area I.



**Somatosensory Area II**

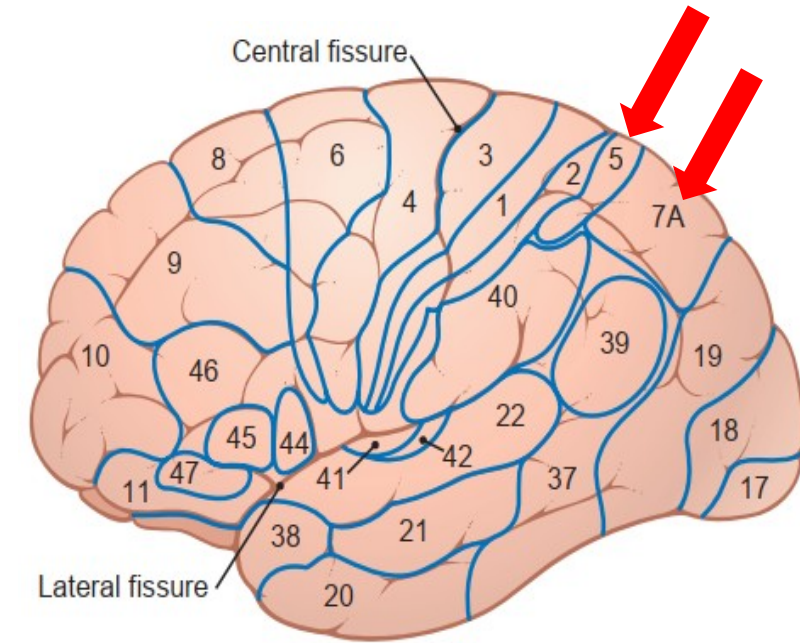


**Brodmann's areas; S II**

# Somatosensory association area



<b>Location</b>	in the parietal cortex behind somatosensory area I and above somatosensory area II
<b>Brodmann's areas</b>	5, 7
<b>Function</b>	-Play important roles in deciphering deeper meanings of the sensory information in the somatosensory areas. It combines information arriving from multiple points in the primary somatosensory area to decipher its meaning.
<b>Effect of its lesion</b>	<ol style="list-style-type: none"> <li>1. Loss of the ability to recognize complex objects felt by the opposite side of the body (<b><u>astereognosis</u></b>).</li> <li>2. Loss of the sense of form of his or her own body or body parts on the opposite side. In fact, the person is mainly forgetting the opposite side of the body. Therefore, the person also often forgets to use the other side for motor functions as well. Likewise, when feeling objects, the person tends to recognize only one side of the object and forgets that the</li> </ol>



**Brodmann's areas; area 5,7**

# Effect of Somatosensory Area I Lesion



Widespread unilateral lesion of somatosensory area I causes loss of the following types of sensations on the ***contralateral*** side of the body.

- ***Loss of fine sensations:***

1. Tactile localization and discrimination.
2. Pressure (To judge the weights of objects).
3. Vibration.
4. Proprioception.
5. Stereognosis (To judge shapes or forms of objects). This condition is called ***astereognosis***.
6. Texture of materials.

***Note that in the list nothing has been said about loss of pain and temperature sense. In the specific absence of only somatosensory area I, appreciation of these sensory modalities is still preserved both in quality and intensity. However, the sensations are poorly localized, indicating that pain and temperature localization depend greatly on the topographical map of the body in somatosensory area I to localize the source.***



# Effect of the Somatosensory Association Area Lesion



1. Loss of the ability to recognize complex objects felt by the opposite side of the body (**astereognosis**).
2. Loss of the sense of form of his or her own body on the opposite side. In fact, the person is mainly forgetting the opposite side of the body. Therefore, the person also often forgets to use the other side for motor functions as well. Likewise, when feeling objects, the person tends to recognize only one side of the object and forgets that the other side even exists (**amorphosynthesis = unilateral neglect**).

# Somatosensory cortex (Quiz)



## Complete:

Left sided lesion in somatosensory area I is presented by loss of

Fine  
touch

Deep  
pressure

Stereogn  
osis

Vibratio  
n

Propriocept  
ion

Pain

Temperat  
ure

Right

with poor localization of..... on the

..... side of

Astereogn  
osis

Amorphosynthesis = Unilateral  
neglect

contralat  
eral

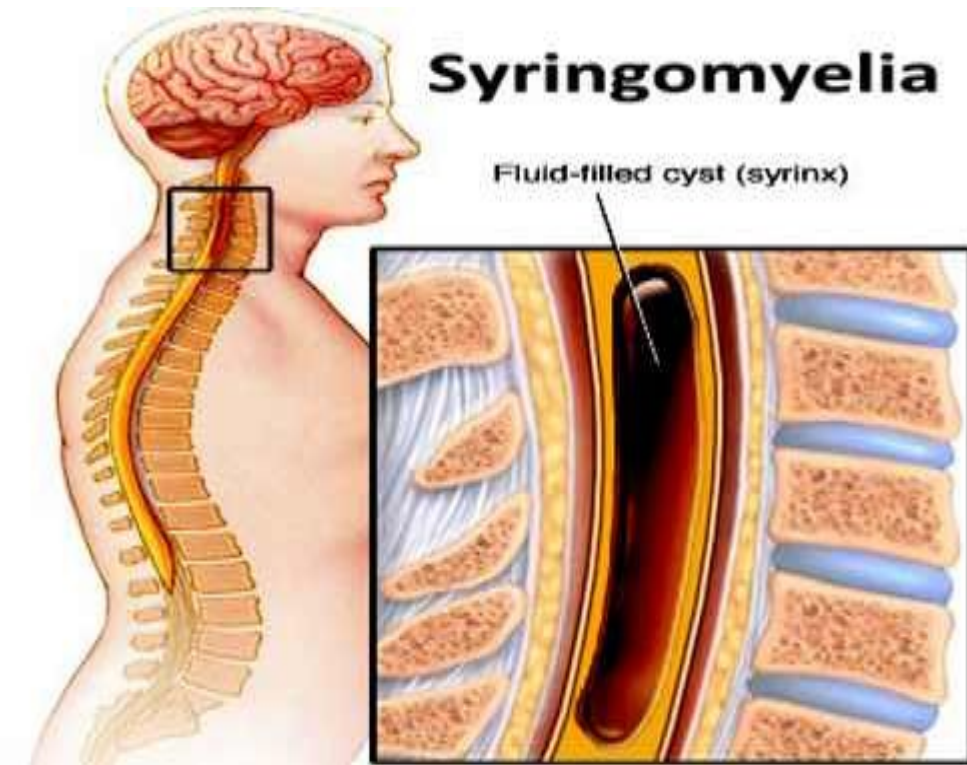
the body. While lesion in somatosensory association area leads to

# Sensory Lesions

## DISEASES ASSOCIATED WITH SENSORY) (DISTURBANCES *SYRINGOMYELIA*



- Congenital in origin.
- Slowly progressive disease.
- Manifestations start to appear at middle ages.
- Affecting mainly females.
- There is an abnormal overgrowth of neuroglial tissue (= gliosis) associated with cavitation around the central canal of the spinal cord.
- Affect lower cervical, upper thoracic region of spinal cord.
- The lesion may extend upwards in the brain stem, resulting in syringo-bulbia.



# Sensory Lesions

## DISEASES ASSOCIATED WITH SENSORY) (DISTURBANCES *SYRINGOMYELIA*



- **Manifestations:**

- (1) **Dissociated sensory loss** "*jacket distribution*".
- (2) Bilateral muscle paralysis at the level of the lesion of **LMNL**
- (3) Unilateral or bilateral **Horner's** syndrome.
- (4) Weakness (or paralysis) of the lower limb muscles of **UMNL**.
- (5) **Syringo-bulbia**.

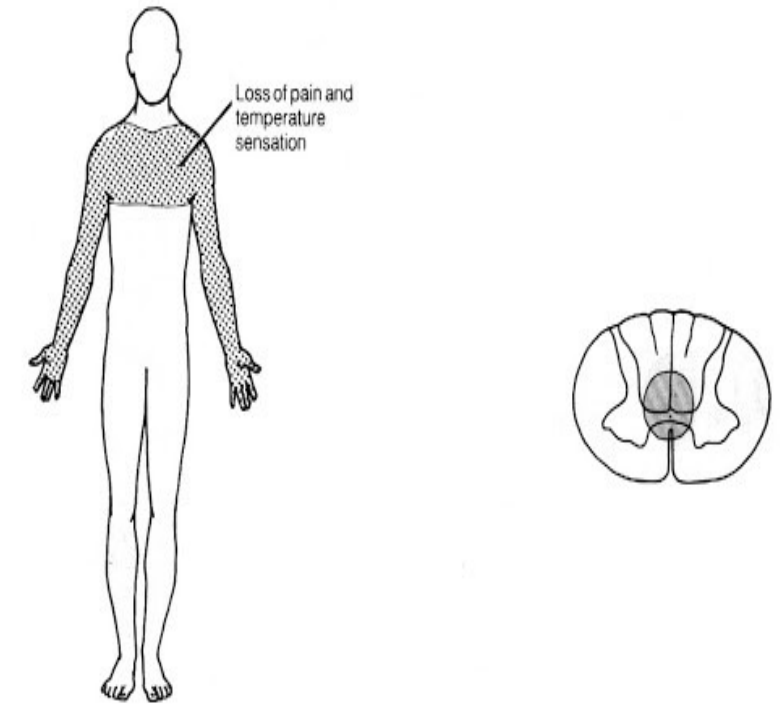


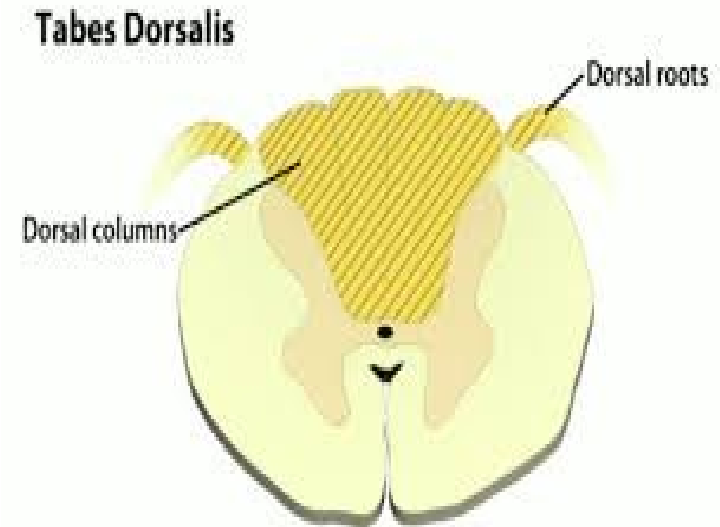
Figure 5-17. Syringomyelia involving the cervicothoracic portion of the spinal cord.

# Sensory Lesions

## DISEASES ASSOCIATED WITH SENSORY (DISTURBANCES *TABES DORSALIS*



- Late stage of *neurosyphilis*.
- Inflammation of the posterior (or dorsal) nerve roots.
- Commonly *bilateral*.
- *At lower thoracic or lumbosacral regions of the spinal cord.*
- Affect both males and females.



# Sensory Lesions

## DISEASES ASSOCIATED WITH SENSORY (DISTURBANCES

### *TABES DORSALIS*



### *Manifestations:*

**Early:**

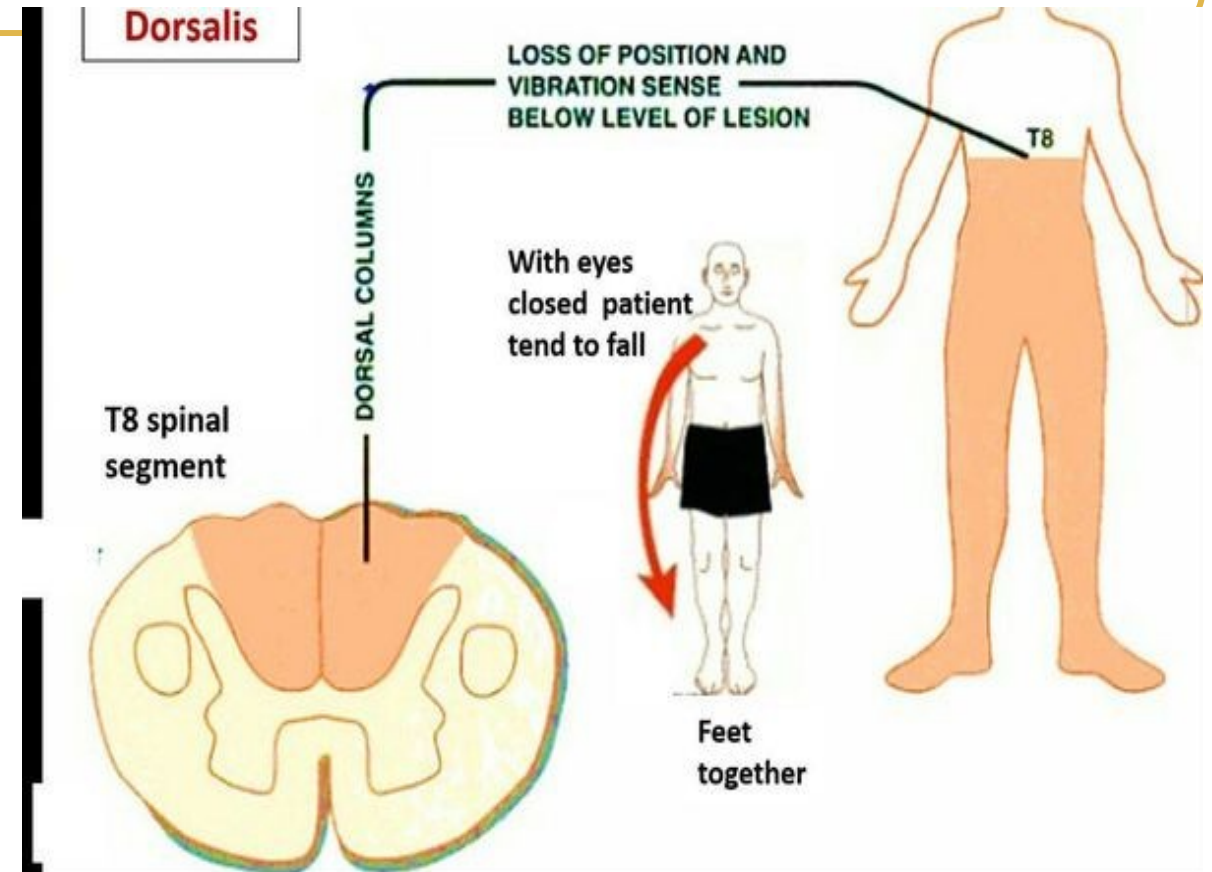
**(1) Attacks of severe lancinating sharp pain**

**(2) Degeneration of the gracile and cuneate tracts:**

- 1- Loss of the fine tactile sensations and the vibration sense.
- 2- Loss of proprioception (sensory ataxia) which is characterized by:

a- The patient walks at a broad base and finds difficulty in walking.

b- Romberg's sign.





# Sensory Lesions

## DISEASES ASSOCIATED WITH SENSORY) (DISTURBANCES

### *TABES DORSALIS*



#### **Manifestations:**

**Late:**

**(1) Loss of all sensations,** but *slow pain remains intact.*

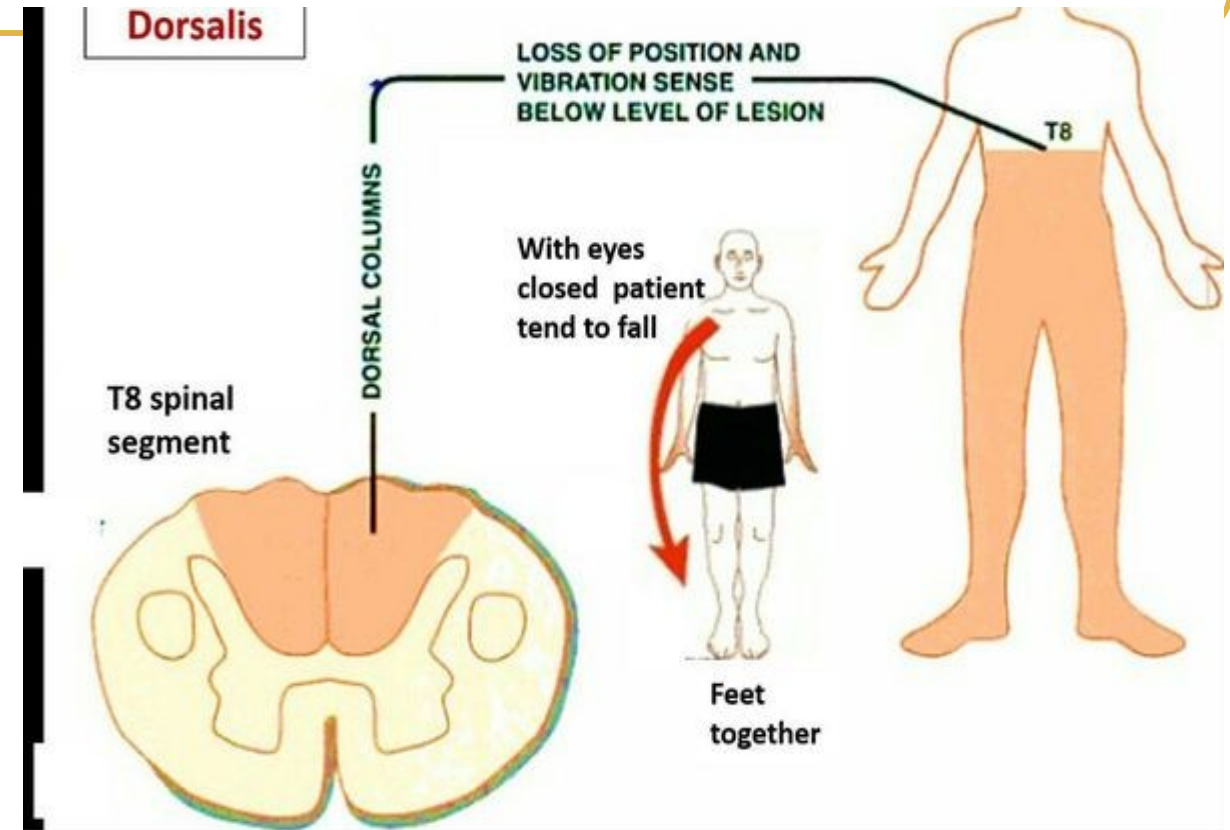
#### **(2) Loss of reflexes:**

(a) *Superficial* reflexes e.g. the withdrawal reflex

(b) *Deep* reflexes e.g. the stretch reflex

(c) *Visceral* reflexes e.g. micturition reflex □ retention with overflow.

**(3) At the terminal stage,** damage of the ***pretectal area*** in the midbrain leading to the Argyll-Robertson pupil.



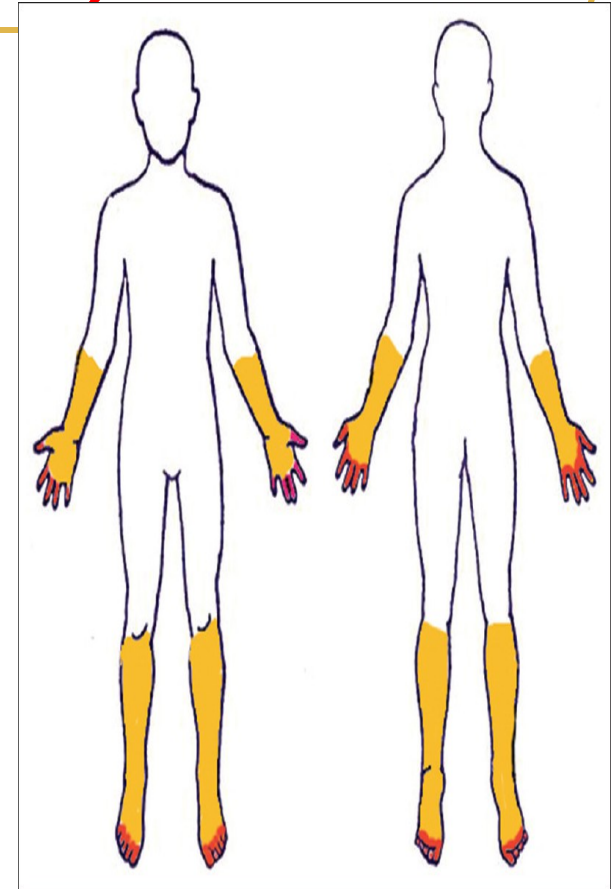
# Sensory Lesions

## DISEASES ASSOCIATED WITH SENSORY) (DISTURBANCES



### ***POLYNEURITIS (PERIPHERAL NEURITIS)***

- Also called polyneuropathy *or peripheral neuropathy*.
- It is characterized by widespread bilateral symmetrical degeneration of the peripheral nerves in the limbs (including both **sensory** and **motor** nerves), and some **cranial** nerves may also be affected.





# Sensory Lesions

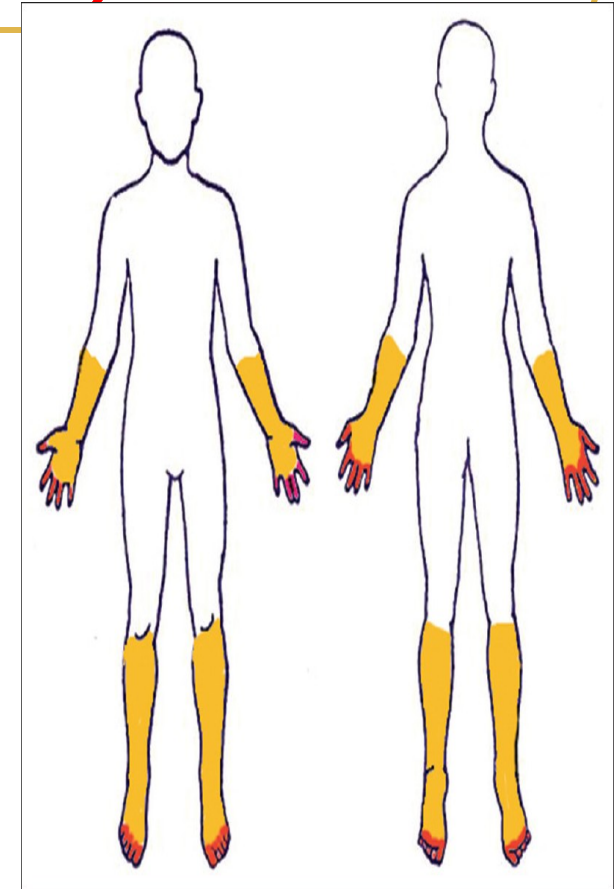
## DISEASES ASSOCIATED WITH SENSORY (DISTURBANCES



### ***POLYNEURITIS (PERIPHERAL NEURITIS)***

#### • ***Causes***

1. Vitamin B deficiency, particularly vitamin B1 (thiamine).
2. Certain metabolic disturbances (e.g. diabetes mellitus).
3. Toxic causes whether endogenous (e.g. uremia) or exogenous (e.g. lead, mercury and arsenic poisoning).
4. Nerve infection by certain viruses or bacteria (e.g. leprosy and tetanus).
5. Some endocrine diseases (e.g. hyperthyroidism and acromegaly).



# Sensory Lesions

## DISEASES ASSOCIATED WITH SENSORY) (DISTURBANCES



### ***POLYNEURITIS (PERIPHERAL NEURITIS)***

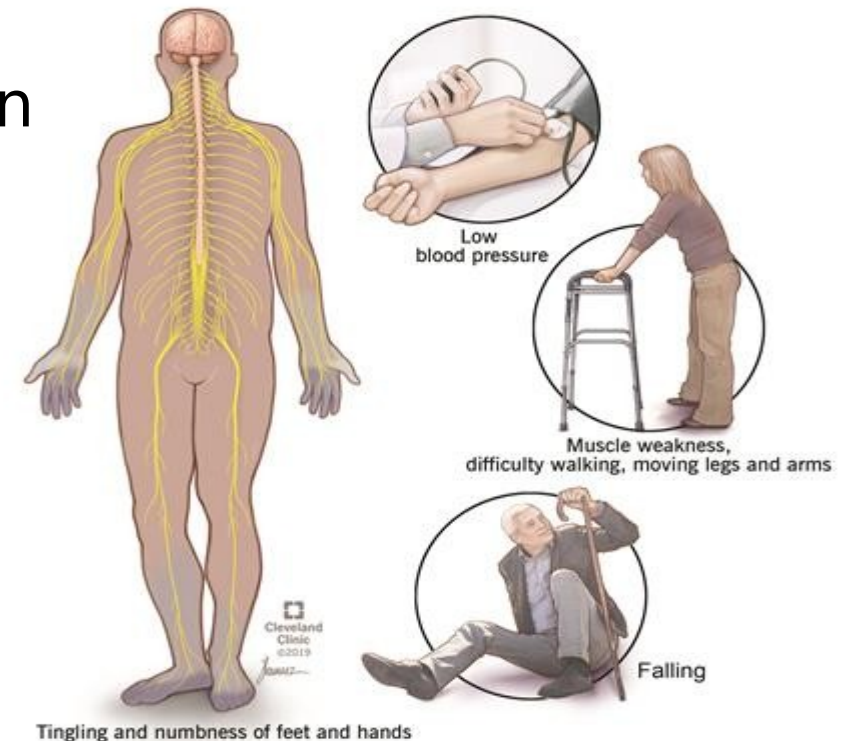
#### ***Manifestations***

##### **(I) Sensory disturbances:**

- At first there is **paresthesia** (sensation of pin pricking, burning, numbness or tingling). Later, **anesthesia** taking a glove and stocking distribution.
- The superficial and deep sensations are also lost, and the latter leads to sensory ataxia.

**(2) Motor disturbances:** Bilateral lower motor neuron lesion (LMNL) and loss of the superficial and deep reflexes.

Some common symptoms of neuropathy



# Sensory Lesions

## DISEASES ASSOCIATED WITH SENSORY) (DISTURBANCES



### ***HERPES ZOSTER (SHINGLES)***

- Viral infection.
- Affecting dorsal root ganglia especially of the thoracic nerves.
- Leads to severe segmental pain that circles halfway around the body with skin vesicular eruption (skin rash of small vesicles) at corresponding dermatomal areas.



Shingles

ADAM

# Sensory Lesions (Quiz)



**A 50-year-old woman undergoes a neurologic exam that indicates poor localization of pain and temperature sensitivity, vibratory sense, and proprioception in the left leg. These symptoms could be explained by:**

- A. a tumor on the right medial lemniscal pathway in the sacral spinal cord.
- B. a tumor on the left medial lemniscal pathway in the sacral spinal cord.
- C. a tumor affecting the right lateral aspect of post-central gyrus.
- D. a tumor affecting the right medial aspect of post-central gyrus.
- E. a large tumor in the right lumbar ventrolateral spinal cord.
- F. a peripheral neuropathy.

# Summary



- Neuropathic pain is an excruciating chronic pain due to nerve damage associated with hyperalgesia and allodynia e.g. peripheral neuritis, phantom limb pain, post-herpetic neuralgia, entrapment neuropathy and causalgia.
- Transmission in pain pathways is modulated by endogenous opioids that can act in the PAG, brainstem, spinal cord. Descending pain modulating pathways include neurons in the PAG, nucleus raphe magnus, and locus coeruleus. Pain analgesia system includes both peripheral and central pathways.
- Somatosensory area I is the site of perception of all fine epicritic sensations. Somatosensory association area is important for stereognosis.
- Sensory lesions e.g. peripheral neuropathy is characterized by tingling and numbness followed by sensory loss with glove and stock distribution, syringomyelia is characterized by dissociated sensory loss with jacket like distribution due to affection of lower cervical upper thoracic spinal cord region, tabes dorsalis characterized by lancinating severe pain initially followed by chronic slow pain affecting the lower limbs due to affection of the lumbosacral region of spinal cord, herpes zoster is characterized by severe neuropathic pain with dermatomal distribution commonly thoracic.



**The terminals of nociceptive afferents release which one of the following transmitters?**

- a. Substance P
- b. Gamma aminobutyric acid (GABA)
- c. Enkephalins
- d. Serotonin
- e. Acetylcholine

# Lecture Quiz



**A neuroscientist wanted to design an experiment to investigate the brain mechanisms that regulate pain. He discovered that, when electrical stimulation was applied to the midline of the medulla, pain sensation was attenuated. Which of the following possibilities could account for this observation?**

- a. Release of serotonin in the dorsal horn of spinal cord.
- b. Release of acetylcholine in the substantia gelatinosa.
- c. Release of norepinephrine from the central processes of dorsal root ganglion cells.
- d. Increased release of substance P from the central processes of dorsal root ganglion cells.
- e. Inhibition of enkephalinergic interneurons in the substantia gelatinosa.

## SUGGESTED TEXTBOOKS



1. Ganong 25<sup>th</sup> edition pages:165-166 & 170 & 172- 174
2. Guyton 13<sup>th</sup> edition from page 611 to 614
3. Siegel Essential Neuroscience 3<sup>rd</sup> edition pages: 256-258